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46298.GB01/NT

0313721.3

2. Patent application number

(The Patent Office will fill in this part) 13 JUN 20033. Full name, address and postcode of the or of each applicant *(underline all surnames)*The Babraham Institute
Babraham Hall
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United KingdomPatents ADP number *(if you know it)*

If the applicant is a corporate body, give the country/state of incorporation

United Kingdom

741459002

4. Title of the invention

Differential Gene Expression in
Schizophrenia

5. Full name, address and postcode in the United Kingdom to which all correspondence relating to this form and translation should be sent

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91001

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Description 39

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Reddie & Grose

13 June 2003

12. Name and daytime telephone number of person to contact in the United Kingdom

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46298.GB01

Differential Gene Expression in Schizophrenia

This invention relates to methods of identifying potential therapeutic agents for the prevention, treatment, or amelioration of schizophrenia (SZ), to methods of diagnosis of schizophrenia, and to methods of prevention, treatment, or amelioration of schizophrenia.

SZ is a severe psychiatric disorder characterized by hallucinations, delusions, disorganized thought, and various cognitive impairments. Polygenic models of inheritance and linkage analysis studies have postulated that several genes confer susceptibility to SZ. Hakak *et al* (PNAS, 2001, 98 (8) 4746-4751) have reported that the expression levels of genes involved in neuronal myelination, development, synaptic plasticity, neurotransmission, and signal transduction were altered in the dorsolateral prefrontal cortex of SZ brain tissue. Mimmack *et al* (PNAS, 2002, 99 (7) 4680-4685) have found significant up-regulation of several members of the apolipoprotein L family in the prefrontal cortex of schizophrenia brains. Middleton *et al* (Journal of Neuroscience, 2002, 22 (7) 2718-2729) have identified alterations of specific metabolic pathways in schizophrenia. However, the molecular basis of schizophrenia is only beginning to be understood. This has hampered development of effective treatments for schizophrenia, and reliable diagnosis of the disorder.

We have identified abnormalities in the expression levels of several genes in the prefrontal cortex of patients with schizophrenia compared with control samples. In particular, the expression level of the following genes was observed to be decreased in the prefrontal cortex of schizophrenia patients:

PARG; OLR1; ARPC3; ARPC3; DNCL1; PPM1A; ATP1F1; TIMM17A; DNAJA1; SST; NEUROD6; ICAP-1A; FLJ23251; KCNK1; FLJ13611; HIRIP5; TAC1; MAGEH1; C13orf12; EBNA1BP2; DIRAS2; MPPE1;

Ornithine related genes: OAT; OAZIN; OAZ2;

Arginine related genes: ARG2;

ATP synthase (mitochondrial) genes: ATP6V1B2; ATP6IP2; ATP6V1C1;

ATP synthase (vacuolar) genes: ATP5J; ATP5G3; ATP5L; ATP5C1; ATP5F1;

ATP5A1;

Complex 1 genes: NDUFAS5; NDUFAS6; NDUFAB1; NDUFB3; NDUFB6; NDUFB5;
 NDUFBI; NDUF54; NDUFAS4; NDUF2C; NDUFB4;
 Complex 3 genes: UQCRH; UQCRFS1; UQCRC2; UQCRB; UQCRC2;
 Complex 4 genes: COX7A2; COX7B; COX5A; COX17; COX11; COX7CP1;
 COX7BP1;
 Holocytochrome c Synthetase genes: HCCS;
 Adenine translocators genes: SLC25A4
 Voltage dependent anion channels (in mitochondrial outer-membrane) genes:
 VDAC2; VDAC1P; VDAC3;
 Lactate metabolism genes: LDHB; LDHA;
 Isocitrate dehydrogenase genes: IDH3B; IDH3A
 HMG related genes: HMGCR
 Glutamate metabolism genes: GLRX2.

The expression level of the following genes was observed to be increased in the prefrontal cortex of schizophrenia patients:

FBS1; WFS1; PRODH; AMT; CLN3; ACOX1; G6PD; GCDH; COL5A1; NY-REN-
 24; TXNL2; SOD3; BCAT2;
 purine metabolism (matrix) genes: ALDH4A1; PYCR1;
 metallo proteins genes: MT1X; MT1L; MT1G; MT1H; MT2A; MT1E; MT1F;
 Arginine related genes: DDAH2;
 Glycine/Serine metabolism genes: AMT;
 HMG related genes: HMGCL;
 Oxide related genes: EPHX1.

Table 1 gives the fold changes in expression of the above genes in the prefrontal cortex of schizophrenia brains compared with control samples, and includes Unigene, ReSeq, and Genbank details, and descriptions of the genes, including synonyms.

Many of the changes are mitochondrial changes. These are illustrated schematically in Figure 1. The changes include changes in ROS stress systems (see the Example).

We have appreciated that these abnormalities can be used to identify potential therapeutic agents for the prevention, treatment, or amelioration of schizophrenia, and for the diagnosis of schizophrenia or susceptibility to schizophrenia.

According to the invention there is provided use of any of the following in a screening assay to identify a potential therapeutic agent for the prevention, treatment, or amelioration of schizophrenia:

(i) proteins encoded by the following genes: PARG; OLR1; ARPC3; ARPC3; DNCL1; PPM1A; ATP1F1; TIMM17A; DNAJA1; SST; NEUROD6; ICAP-1A; FLJ23251; KCNK1; FLJ13611; HIRIP5; TAC1; MAGEH1; C13orf12; EBNA1BP2; DIRAS2; MPPE1; OAT; OAZIN; OAZ2; ARG2; ATP6V1B2; ATP6IP2; ATP6V1C1; ATP5J; ATP5G3; ATP5L; ATP5C1; ATP5F1; ATP5A1; NDUFA5; NDUFA6; NDUFAB1; NDUFB3; NDUFB6; NDUFB5; NDUFB1; NDUFS4; NDUFA4; NDUF2; NDUFB4; UQCRH; UQCRFS1; UQCRC2; UQCRB; UQCRC2; COX7A2; COX7B; COX5A; COX17; COX11; COX7CP1; COX7BP1; HCCS; SLC25A4; VDAC2; VDAC1P; VDAC3; LDHB; LDHA; IDH3B; IDH3A; HMGCR; GLRX2; FBS1; WFS1; PRODH; AMT; CLN3; ACOX1; G6PD; GCDH; COL5A1; NY-REN-24; TXNL2; SOD3; BCAT2; ALDH4A1; PYCR1; MT1X; MT1L; MT1G; MT1H; MT2A; MT1E; MT1F; DDAH2; AMT; HMGCL; EPHX1; or

ii) nucleic acid encoding any of the proteins of (i) above.

There is also provided according to the invention use of a regulator of expression of any of (i) above, in a screening assay to identify a potential therapeutic agent for the prevention, treatment, or amelioration of schizophrenia.

There is further provided according to the invention use of a binding partner of any of (i) above in a screening assay to identify a potential therapeutic agent for the prevention, treatment, or amelioration of schizophrenia.

According to the invention there is also provided use of an expression vector comprising nucleic acid encoding any of (i) above in a screening assay to identify a potential therapeutic agent for the prevention, treatment, or amelioration of schizophrenia.

There is further provided according to the invention use of a cell or cell line expressing nucleic acid encoding any of (i) above in a screening assay to identify a potential therapeutic agent for the prevention, treatment, or amelioration of schizophrenia. Preferably the cell is a neural cell, or an oligodendrocyte.

There is also provided according to the invention a recombinant mouse in which expression of a gene encoding any of the proteins of (i) above is altered compared with expression of the corresponding gene in normal mice. Preferably

expression of two or more of the genes is altered. Expression of the gene or genes in the recombinant mouse may be increased or decreased. Where expression is decreased, preferably the mouse is a knockout mouse for the gene or genes.

Preferably expression of PARG; OLR1; ARPC3; ARPC3; DNCL11; PPM1A; ATP1F1; TIMM17A; DNAJA1; SST; NEUROD6; ICAP-1A; FLJ23251; KCNK1; FLJ13611; HIRIP5; TAC1; MAGEH1; C13orf12; EBNA1BP2; DIRAS2; MPPE1; OAT; OAZIN; OAZ2; ARG2; ATP6V1B2; ATP6IP2; ATP6V1C1; ATP5J; ATP5G3; ATP5L; ATP5C1; ATP5F1; ATP5A1; NDUFA5; NDUFA6; NDUFAB1; NDUFB3; NDUFB6; NDUFB5; NDUFB1; NDUFS4; NDUFA4; NDUFC2; NDUFB4; UQCRH; UQCRFS1; UQCRC2; UQCRB; UQCRC2; COX7A2; COX7B; COX5A; COX17; COX11; COX7CP1; COX7BP1; HCCS; SLC25A4; VDAC2; VDAC1P; VDAC3; LDHB; LDHA; IDH3B; IDH3A; HMGCR; GLRX2 is decreased in the recombinant mouse.

Preferably expression of FBS1; WFS1; PRODH; AMT; CLN3; ACOX1; G6PD; GCDH; COL5A1; NY-REN-24; TXNL2; SOD3; BCAT2; ALDH4A1; PYCR1; MT1X; MT1L; MT1G; MT1H; MT2A; MT1E; MT1F; DDAH2; AMT; HMGCL; EPHX1 is increased in the recombinant mouse.

The invention also provides use of a recombinant mouse of the invention as an animal model for schizophrenia.

According to the invention there is also provided use of a mouse of the invention, or cells obtained or derived from the mouse, in a screening assay to identify a potential therapeutic agent for the prevention, treatment, or amelioration of schizophrenia.

A screening assay for identifying a potential therapeutic agent for the prevention, treatment, or amelioration of schizophrenia may comprise screening for a modulator of expression of a gene encoding any of the proteins of (i) above by: providing a system capable of expressing a gene encoding any of the proteins of (i) above; maintaining the system under conditions for expression of the gene in the presence and absence of a candidate modulator of expression of the gene; and determining the expression level of the gene in the presence and absence of the candidate modulator.

An upregulator of expression of any of the following is expected to provide a potential therapeutic agent for the prevention, treatment, or amelioration of

schizophrenia: PARG;OLR1; ARPC3; ARPC3; DNCL1; PPM1A; ATP1F1;
TIMM17A; DNAJA1; SST; NEUROD6; ICAP-1A; FLJ23251; KCNK1; FLJ13611;
HIRIP5; TAC1; MAGEH1; C13orf12; EBNA1BP2; DIRAS2; MPPE1; OAT;
OAZIN; OAZ2; ARG2; ATP6V1B2; ATP6IP2; ATP6V1C1; ATP5J; ATP5G3;
ATP5L; ATP5C1; ATP5F1; ATP5A1; NDUFA5; NDUFA6; NDUFAB1; NDUFB3;
NDUFB6; NDUFB5; NDUFB1; NDUFS4; NDUFA4; NDUFC2; NDUFB4;
UQCRRH; UQCRRS1; UQCRC2; UQCRB; UQCRC2; COX7A2; COX7B; COX5A;
COX17; COX11; COX7CP1; COX7BP1; HCCS; SLC25A4; VDAC2; VDAC1P;
VDAC3; LDHB; LDHA; IDH3B; IDH3A; HMGCR; GLRX2.

A downregulator of expression of any of the following is expected to provide a potential therapeutic agent for the prevention, treatment, or amelioration of schizophrenia: FBS1; WFS1; PRODH; AMT; CLN3; ACOX1; G6PD; GCDH; COL5A1; NY-REN-24; TXNL2; SOD3; BCAT2; ALDH4A1; PYCR1; MT1X; MT1L; MT1G; MT1H; MT2A; MT1E; MT1F; DDAH2; AMT; HMGCL; EPHX1.

An alternative screening assay for identifying a potential therapeutic agent for the prevention, treatment, or amelioration of schizophrenia may comprise screening for a regulator of the activity of any of the proteins of (i) above by: contacting the protein with a candidate regulator and determining the activity of the protein in the presence and absence of the candidate regulator.

An enhancer or activator of the activity of any of the following proteins may provide a potential therapeutic agent for the prevention, treatment, or amelioration of schizophrenia: PARG; OLR1; ARPC3; ARPC3; DNCL1; PPM1A; ATP1F1; TIMM17A; DNAJA1; SST; NEUROD6; ICAP-1A; FLJ23251; KCNK1; FLJ13611; HIRIP5; TAC1; MAGEH1; C13orf12; EBNA1BP2; DIRAS2; MPPE1; OAT; OAZIN; OAZ2; ARG2; ATP6V1B2; ATP6IP2; ATP6V1C1; ATP5J; ATP5G3; ATP5L; ATP5C1; ATP5F1; ATP5A1; NDUFA5; NDUFA6; NDUFAB1; NDUFB3; NDUFB6; NDUFB5; NDUFB1; NDUFS4; NDUFA4; NDUFC2; NDUFB4; UQCRRH; UQCRRF1; UQCRC2; UQCRB; UQCRC2; COX7A2; COX7B; COX5A; COX17; COX11; COX7CP1; COX7BP1; HCCS; SLC25A4; VDAC2; VDAC1P; VDAC3; LDHB; LDHA; IDH3B; IDH3A; HMGCR; GLRX2.

An inhibitor of the activity of any of the following proteins may provide a potential therapeutic agent for the prevention, treatment, or amelioration of schizophrenia: FBS1; WFS1; PRODH; AMT; CLN3; ACOX1; G6PD; GCDH;

Examples of suitable methods for determining the level of mRNA expression are quantitative PCR (in particular, real-time quantitative PCR) performed on cDNA produced by reverse transcription of the mRNA, and Northern blotting.

In a preferred method of determining the level of mRNA expressed, total RNA is obtained from the biological sample, cDNA is synthesized from mRNA of the gene, and the cDNA is used for real-time quantitative PCR analysis to determine the level of the mRNA in the sample.

Examples of suitable methods for determining the level of protein expression are Western blotting and enzyme-linked immunosorbent assay (ELISA).

A binding partner of an expression product of the gene, may be used to detect the level of that expression product. The binding partner may be a protein, preferably an antibody or antibody fragment. The antibody or antibody fragment should bind specifically to the expression product so that the level of the expression product in the biological sample can be determined.

The binding partner may be a nucleic acid capable of hybridizing to a nucleic acid expression product of the gene. The nucleic acid should hybridize specifically (for example under conditions of high stringency) to the nucleic acid expression product so that the level of the nucleic acid expression product in the biological sample can be determined. A preferred nucleic acid binding partner is an oligonucleotide primer for the synthesis of cDNA by reverse transcription from mRNA of the gene.

The level of a nucleic acid expression product of the gene is preferably determined by amplification of that nucleic acid expression product, for example by PCR. Thus, primers capable of amplifying the nucleic acid expression product are provided. Nucleic acid capable of hybridizing (preferably under conditions of high stringency) to nucleic acid that is complementary to a nucleic acid expression product of the gene and/or nucleic acid which is a binding partner (preferably under conditions of high stringency) of an expression product of the gene may be used to amplify a nucleic acid expression product of the gene, for example to detect an expression product of the gene.

There is also provided a kit for the diagnosis of schizophrenia that comprises a means for detecting the protein or expression product of a gene encoding the protein. The detecting means may comprise a binding partner of the protein, and/or a nucleic

acid capable of hybridizing to nucleic acid that is complementary to a nucleic acid expression product of the gene.

There is also provided according to the invention a method of diagnosing whether a subject has, or is at risk of developing schizophrenia, which comprises determining the level of any of the proteins of (i), or the expression level of a gene encoding any of the proteins of (i) above, in the brain (preferably the prefrontal cortex) of the subject.

The level of more than one of the proteins of (i) above, or the expression level of more than one of the genes encoding the proteins of (i) above may be determined. This may increase the accuracy of the diagnosis.

If the level of the protein or expression product in the brain is abnormal, the subject is diagnosed as either having schizophrenia, or being at risk of developing schizophrenia.

In particular, the subject is diagnosed as either having schizophrenia, or being at risk of developing schizophrenia, if the level of any of the following proteins, or the expression level of a gene encoding any of the following proteins is reduced compared to a normal subject: PARG; OLR1; ARPC3; ARPC3; DNCL11; PPM1A; ATP1F1; TIMM17A; DNAJA1; SST; NEUROD6; ICAP-1A; FLJ23251; KCNK1; FLJ13611; HIRIP5; TAC1; MAGEH1; C13orf12; EBNA1BP2; DIRAS2; MPPE1; OAT; OAZIN; OAZ2; ARG2; ATP6V1B2; ATP6IP2; ATP6V1C1; ATP5J; ATP5G3; ATP5L; ATP5C1; ATP5F1; ATP5A1; NDUFA5; NDUFA6; NDUFAB1; NDUFB3; NDUFB6; NDUFB5; NDUFB1; NDUFS4; NDUFA4; NDUFC2; NDUFB4; UQCRH; UQCRFS1; UQCRC2; UQCRB; UQCRC2; COX7A2; COX7B; COX5A; COX17; COX11; COX7CP1; COX7BP1; HCCS; SLC25A4; VDAC2; VDAC1P; VDAC3; LDHB; LDHA; IDH3B; IDH3A; HMGCR; GLRX2.

The subject is diagnosed as either having schizophrenia, or being at risk of developing schizophrenia, if the level of any of the following proteins, or the expression level of a gene encoding any of the following proteins is increased compared to a normal subject: FBS1; WFS1; PRODH; AMT; CLN3; ACOX1; G6PD; GCDH; COL5A1; NY-REN-24; TXNL2; SOD3; BCAT2; ALDH4A1; PYCR1; MT1X; MT1L; MT1G; MT1H; MT2A; MT1E; MT1F; DDAH2; AMT; HMGCL; EPHX1.

There is further provided according to the invention a method of prevention, treatment, or amelioration of schizophrenia which comprises increasing the level or activity of any of the following proteins in the brain (in particular the prefrontal cortex) of a subject in need of such prevention, treatment, or amelioration: PARG; OLR1; ARPC3; ARPC3; DNCL1; PPM1A; ATP1F1; TIMM17A; DNAJA1; SST; NEUROD6; ICAP-1A; FLJ23251; KCNK1; FLJ13611; HIRIP5; TAC1; MAGEH1; C13orf12; EBNA1BP2; DIRAS2; MPPE1; OAT; OAZIN; OAZ2; ARG2; ATP6V1B2; ATP6IP2; ATP6V1C1; ATP5J; ATP5G3; ATP5L; ATP5C1; ATP5F1; ATP5A1; NDUFA5; NDUFA6; NDUFAB1; NDUFB3; NDUFB6; NDUFB5; NDUFB1; NDUFS4; NDUFA4; NDUFC2; NDUFB4; UQCRC1; UQCRC2; UQCRB; UQCRC2; COX7A2; COX7B; COX5A; COX17; COX11; COX7CP1; COX7BP1; HCCS; SLC25A4; VDAC2; VDAC1P; VDAC3; LDHB; LDHA; IDH3B; IDH3A; HMGCR; GLRX2.

There is also provided according to the invention a method of prevention, treatment, or amelioration of schizophrenia which comprises reducing the level or activity of any of the following proteins in the brain (in particular the prefrontal cortex) of a subject in need of such prevention, treatment, or amelioration: FBS1; WFS1; PRODH; AMT; CLN3; ACOX1; G6PD; GCDH; COL5A1; NY-REN-24; TXNL2; SOD3; BCAT2; ALDH4A1; PYCR1; MT1X; MT1L; MT1G; MT1H; MT2A; MT1E; MT1F; DDAH2; AMT; HMGCL; EPHX1.

The level of a protein may be altered by gene therapy. The level of a protein may be altered by use of a regulator of expression of a gene coding for the protein.

Experiments which are the basis of the invention are described in the following example, with reference to the accompanying drawings in which:

Figure 1 shows mitochondrial changes associated with schizophrenia;

Figure 2 shows sample quality control steps;

Figure 3 shows data quality control steps;

Figures 4 and 5 show clustering analysis between control (C) and schizophrenia (S) samples; and

Figure 6 shows oxidative buffering.

Example

**Integrating Transcriptomics, Proteomics, and Classical Genetics:
Fishing in modern neuropsychiatric research**

**Affymetrix® GeneChip® Post-Mortem
Brain Studies**

HG-U133 set includes:

- 39,000 probes
- 33,000 annotated
- 2 chips: A and B
- Each w/ ~23,000 genes on 1.28 cm²

Our Studies:

- 150 PM human brain samples from SMRI
- Completed on HG-U133A chips and continuing on B
- Extensive Quality Control(QC) steps
- Cluster analysis

Sample QC Steps (see Figure 2):

Total RNA is screened for degraded samples

cRNA is generated and screened for poor modal length

- Poor samples are run on Test3 GeneChips®
- Pristine samples are run on U133 GeneChips®

Microarrays are put through our in-house Data QC screen and only "clean" data sets are retained, poor set samples are rerun or rejected

Data QC Steps (see Figure 3):

6 data filters

- RNA digestion plots
- Box plots
- 2 D-chip screens
- In-house parameter script
- In-house heuristic meta-analysis script

Data Mining

- Flag Filtering
- Fold Difference and Significance Filtering
- Subset Significant Gene Overlapping
- Pathway Specific Filtering

Cluster Analysis (see Figures 4 and 5)

Initial Clustering (17,886 genes)

Patients begin to separate ...

Until the trees begin to separate large groups of patients on a large gene scale (392 genes)

Filtering on oxidative stress and mitochondrial genes (35 genes)

- 82% separation for C in S
- 90% separation for S in C

Mitochondrial Involvement: Evidence for ROS stress (see Figure 6)

Oxidative Stress: Evidence for Stress Response

Up-regulations in MT transcripts

Changes in specific ROS stress systems including:

- | | |
|-------------------------|---------------------------|
| — SOD's | — HIF's |
| — MSR | — Fe containing molecules |
| — GLRX | |
| — PDCD's | |
| — Specific RAS pathways | |

Changes in DNA repair mechanisms

Future Directions

- Continue data mining of Affymetrix® results
- Validate gene hits via Q-PCR and poly-"omics"
- Genotyping and SNP analysis of genes that separate patient groups
- GeneChip analysis of peripheral tissues including liver, spleen, blood and duramata

Table 1

Significant clustered 90% separation of schizophrenics from controls	Systematic	Common	Genbank	Map	UniGene	GeneSpring Norm Fold	Test	Down	Test	Down	Test	Description
							S-C				S-C	
205080_at		PARG	NM_003631	10q11.23	Hs.61390	1.510748	Down	3.7332E-03	1.5851727	Down	0.0160633	Homo sapiens poly (ADP-ribose) glycohydrolase (PARG), mRNA.
211682_s_at		VDAC2	U08886	10q22	Hs.78902	1.12617	Down	0.014193997	1.240873	Down	0.052483	Homo sapiens voltage-dependent anion channel 2 (VDAC2), mRNA.
210004_at		OLR1; OLR1; LOX1; LOX-1; SCARE1	AF035775	12p13.2-p12.3	Hs.77729	1.377438	Down	0.044075548	1.2097276	Down	0.0027743	synonyms: LOX1, LOX-1, SCARE1; scavenger receptor class E, member 1; Homo sapiens oxidised low density lipoprotein (lectin-like) receptor 1 (OLR1), mRNA.
208735_at		ARPC3; ARPC3; ARPC21; p21-Arc	AF004551	12q24.11	Hs.29375	1.285561	Down	5.21013E-05	1.1333508	Down	0.042248	synonyms: ARPC21, p21-Arc; ARP2/3 protein complex subunit p21; Homo sapiens actin related protein 2/3 complex, subunit 3, 21kDa (ARPC3), mRNA.
208809_at		UQCRCF31; UQCRCF31; RUS1	BC000649	18q12-q13.1	Hs.3712	1.168573	Down	0.01259279	1.2110709	Down	0.0002244	synonym: RUS1; Homo sapiens ubiquinol-cytochrome c reductase, Rieske iron-sulfur polypeptide 1 (UQCRCF31), nuclear gene encoding mitochondrial protein, mRNA.
217878_s_at		DNCL11	NM_016141		Hs.28948	1.334079	Down	6.56512E-03	1.2676281	Down	0.0023879	Homo sapiens dynein, cytoplasmic, light intermediate polypeptide 1 (DNCL11), mRNA.

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218571_s_at	ATPIF1; ATPIF1; MGC1167; MGC8898	NM_016911	1p35.3	Hs.24133 6	1.155111	Down	0.015292848	1.155271	Down	0.0153928	synonyms: MGC8898, MGC1167, ATPi; isoform 1 is encoded by transcript variant 1; Homo sapiens ATPase inhibitory factor 1 (ATPIF1), transcript variant 1, nuclear gene encoding mitochondrial protein, mRNA; synonyms: MGC8898, MGC1167, ATPi; isoform 2 is encoded by transcript variant 2; Homo sapiens ATPase inhibitory factor 1 (ATPIF1), transcript variant 2, nuclear gene encoding mitochondrial protein, mRNA; synonyms: MGC8898, MGC1167, ATPi; isoform 3 is encoded by transcript variant 3; Homo sapiens ATPase inhibitory factor 1 (ATPIF1), transcript variant 3, nuclear gene encoding mitochondrial protein, mRNA.
219933_at	GLRX2; GLRX2; GRX2	NM_016066	1q31.2- q31.3	Hs.5054	1.214851	Down	0.000850749	1.237224	Down	0.0001632	synonym: GRX2; thioltransferase; contains nuclear membrane localization; CGI-133 protein; Homo sapiens glutaredoxin 2 (GLRX2), mRNA.
215171_s_at	TIMM17A; TIMM17A; TIM17; TIM17A	AK023063	1q32.1	Hs.20716	1.223886	Down	0.000427331	1.2024004	Down	0.0004325	synonyms: TIM17, TIM17A; preprotein translocase; Homo sapiens translocase of inner mitochondrial membrane 17 homolog A (yeast) (TIMM17A), mRNA.

210418_s_at	IDH3B; IDH3B; H-IDHB; MGC903; FLJ11043	AF023285	20p13	Hs.15541 0	1.167603 Down	0.008473711	1.1632137 Down	0.0086675	synonyms: H-IDHB, MGC903, FLJ11043; isocitric dehydrogenase; NAD+-specific isocitrate dehydrogenase beta precursor; NAD+-specific isocitrate dehydrogenase b subunit; NAD+-specific ICDH; isocitrate dehydrogenase, NAD(+)-specific, mitochondrial, beta subunit; Homo sapiens isocitrate dehydrogenase 3 (NAD+) beta (IDH3B), nuclear gene encoding mitochondrial protein, transcript variant 1, mRNA.
203948_s_at	ARG2	U75687	14q24.1- q24.3	Hs.17285 1	1.241001 Down	0.004931689	1.1754939 Down	0.0066619	kidney arginase; nonhepatic arginase; L-arginine amidohydrolase; L-arginine ureahydrolase; A-II; Homo sapiens arginase, type II (ARG2), nuclear gene encoding mitochondrial protein, mRNA.
200880_at	DNAJA1	AL534104	9p13-p12	Hs.94	1.255564 Down	0.006175319	1.2076039 Down	3.252505	DnaJ (Hsp40) homolog, subfamily A, member 1
213821_at	SST; SST; SMST	NM_001046	3q28	Hs.12409	1.515051 Down	0.000215427	1.538134 Down	7.912E-05	synonym: SMST; Homo sapiens somatostatin (SST), mRNA.

210014_x_at	IDH3B; IDH3B; H-IDHB; MGC303; FLJ11043	AF023268	20p13	Hs.15541 0	1.123501 Down	2.018203253	1.121091 Down	0.01016	synonyms: H-IDHB, MGC303, FLJ11043; isocitric dehydrogenase; NAD+-specific isocitrate dehydrogenase beta precursor; NAD+-specific isocitrate dehydrogenase b subunit; NAD+-specific IDH; isocitrate dehydrogenase, NAD(+)-specific, mitochondrial, beta subunit; Homo sapiens isocitrate dehydrogenase 3 (NAD+) beta (IDH3B), nuclear gene encoding mitochondrial protein, transcript variant 1, mRNA.
220045_at	NEUROD6; NEUROD6; Atah2; NEX1M; Math-2	NM_022728		Hs.45152	1.263805 Down	0.008516781	1.3729238 Down	8.878E-03	synonyms: Atah2, NEX1M, Math 2; Homo sapiens neurogenic differentiation 6 (NEUROD6), mRNA.
203336_p_at	ICAP-1A	AL548353	2p25.2	Hs.17327 4	1.316161 Down	0.000468987	1.3671768 Down	1.918E-05	integrin cytoplasmic domain- associated protein 1
218289_s_at	FLJ23251	NM_024518	3q22.1	Hs.17073 7	1.15484 Down	0.022580668	1.1592488 Down	0.0080202	Homo sapiens hypothetical protein FLJ23251 (FLJ23251), mRNA.
204879_at	KCNK1; KCNK1; DPK; HOHO; TWIK1; TWIK-1	NM_002245	1q42-q43	Hs.79351	1.253524 Down	0.00034664	1.2886284 Down	3.352E-05	synonyms: DPK, HOHO, TWIK1, TWIK-1; potassium inwardly-rectifying channel, subfamily K, member 1; potassium channel, subfamily K, member 1 (TWIK-1); Homo sapiens potassium channel, subfamily K, member 1 (KCNK1), mRNA.

202825_at	SLC25A4; SLC25A4; T1; ANT; ANT1; PEO2; PEO3	NM_001151	4q35	Hs.2343	1.243055	Down	0.003755793	1.1702688	Down	0.004138	synonyms: T1, ANT, ANT1, PEO2, PEO3; adenine nucleotide translocator 1 (skeletal muscle); Homo sapiens solute carrier family 25 (mitochondrial carrier, adenine nucleotide translocator), member 4 (SLC25A4), nuclear gene encoding mitochondrial protein, mRNA.
218674_at	FLJ13611	NM_024941	5q12.2	Hs.28295 8	1.280891	Down	3.93072E-05	1.1687684	Down	0.0110843	Homo sapiens hypothetical protein FLJ13611 (FLJ13611), mRNA.
218846_at	HIRIP5; HIRIP5; CGI-33	NM_015700	2p15-p13	Hs.43043 9	1.20213	Down	0.000350468	1.2521308	Down	0.482E-05	synonym: CGI-33; HIRIP5 protein; HIRA-interacting protein 5; Homo sapiens HIRA interacting protein 5 (HIRIP5), mRNA.
201597_at	COX7A2; COX7A2; COX7AL; COX7AL1; COXVIIa-L	NM_001865	8q12	Hs.70312	1.149356	Down	0.00765477	1.182428	Down	1.847E-05	synonyms: COX7AL, COX7AL1, COXVIIa-L; hepatic cytochrome- c oxidase chain VIIa; Homo sapiens cytochrome c oxidase subunit VIIa polypeptide 2 (liver) (COX7A2), nuclear gene encoding mitochondrial protein, mRNA.
203663_s_at	COX5A; COX5A; VA; COX-VA	NM_004255	16q25	Hs.32383 4	1.197943	Down	0.004379027	1.2294325	Down	7.346E-09	synonyms: VA, COX, COX-VA; cytochrome c oxidase polypeptide, mitochondrial precursor, Homo sapiens cytochrome c oxidase subunit Va (COX5A), nuclear gene encoding mitochondrial protein, mRNA.

208552_a_at	TAC1; TAC1; NIK2; NKNA; TAC2	NM_003182	7q21-q22	Hs.2553	1.562809	Down	2.272815-07	1.5689365	Down	2.145E-06	synonyms: NIK2, NKNA, TAC2; neurokinin A; neurokinin alpha; tachykinin 2; substance K; neuropeptide K; neuropeptide gamma; substance P; neurokinin 1; neurokinin 2; neuromedin L; Homo sapiens tachykinin, precursor 1 (substance K, substance P, neurokinin 1, neurokinin 2, neuromedin L, neurokinin alpha, neuropeptide K, neuropeptide gamma) (TAC1), transcript variant beta, mRNA; synonyms: NIK2, NKNA, TAC2; neurokinin A; neurokinin alpha; tachykinin 2; substance K; neuropeptide K; neuropeptide gamma; substance P; neurokinin 1; neurokinin 2; neuromedin L; Homo sapiens tachykinin, precursor 1 (substance K, substance P, neurokinin 1, neurokinin 2, neuromedin L, neurokinin alpha, neuropeptide K, neuropeptide gamma) (TAC1), transcript variant alpha,
202233_a_at	UQCRH	NM_006004		Hs.73918	1.148508	Down	0.025106627	1.1682167	Down	2.697E-05	Homo sapiens ubiquinol- cytochrome c reductase hinge protein (UQCRH), mRNA
218573_at	MAGEH1; MAGEH1; APR- 1	NM_014051	Xp11.22	Hs.27931 9	1.167834	Down	0.018662032	1.2202681	Down	8.034E-05	synonym: APR-1; refseq: MAGE- H1 antigen; Homo sapiens APR- 1 protein (MAGEH1), mRNA.

217769_s_at	C13orf12; C13orf12; HSPC014; 2510048006Rik	NM_016932	13q12.13	Hs.27881 3	1.144417	Down	0.009888437	1.1710335	Down	9.8675-05	synonyms: HSPC014, 2510048006Rik; Homo sapiens chromosome 13 open reading frame 12 (C13orf12), mRNA.
201323_at	EBNA1BP2; EBNA1BP2; P40; EBP2; NOBP	NM_006524	1p35-p33	Hs.34895 6	1.13658	Down	0.018139154	1.1888038	Down	4.837E-05	synonyms: P40, EBP2, NOBP; cell proliferation-associated protein; nuclear protein p40; homolog of yeast EBNA1- binding protein; nuclear FGF3 binding protein; EBNA1-binding protein 2; Homo sapiens EBNA1 binding protein 2 (EBNA1BP2), mRNA.
219819_at	DIRAS2; DIRAS2; D1- Ras2; DKFZp761C071 21	NM_017594	9q22.1	Hs.18563 6	1.28122	Down	3.36473E-05	1.2324031	Down	1.828E-05	synonyms: D1-Ras2, DKFZp761C07121; member of the Ras family small GTP- binding protein; Homo sapiens DIRAS family, GTP-binding RAS like 2 (DIRAS2), mRNA.
213824_at	MPPE1	BF478502	18p11.21	Hs.15414 5	1.18484	Down	0.004053387	1.1134946	Down	0.0562816	metallo phosphoesterase
218255_s_at	FBS1; FBS1; FLJ11818	NM_022452	16p11.2	Hs.77735	1.308388	Up	9.96836E-05	1.2807938	Up	4.324E-05	synonyms: FBS, FLJ11818; likely ortholog of mouse fibroblast Homo sapiens fibroblast 1 (FBS1), mRNA.
202808_at	WFS1; WFS1; WFRS; DFNA8; DFNA14; DFNA38; DIDMOAD; WOLFRAMIN	NM_055005	4p16	Hs.28077	1.264458	Up	1.9637E-05	1.2121222	Up	0.0048794	synonyms: WFS, WFRS, DFNA8, DFNA14, DFNA38, DIDMOAD, WOLFRAMIN; Homo sapiens Wolfram syndrome 1 (wolfram) (WFS1), mRNA.
214203_s_at	PRODH	A0074145	22q11.21	Hs.34387 4	1.410083	Up	0.005560916	1.1914316	Up	0.0038675	proline dehydrogenase (oxidase) 1

204294_at	AMT; AMT; (GCE, NKH; GUST	NM_002491	3p21.2- p21.1	Hs.102	1.20589	Up	0.003897535	1.0981119	Up	0.0102842	synonyms: GCE, NKH, GCEST; Homo sapiens aminomethyltransferase (glycine cleavage system protein T) (AMT), mRNA
209275_s_at	CLN3; CLN3; BTS	AF018593	16p12.1	Hs.19455 0	1.194557	Up	0.010213385	1.1280952	Up	0.0775445	synonyms: BTS; Homo sapiens ceroid-lipofuscinosis, neuronal 3, juvenile (Batten, Spielmeyer- Vogt disease) (CLN3), mRNA.
209500_s_at	ACOX1; ACOX1; MGC1198; PALMCOX	S69189	17q24- 17q25	Hs.37859 1	1.271366	Up	0.003205435	1.1650975	Up	0.0599728	synonyms: ACOX, PALMCOX, MGC1198; acyl-coenzyme A oxidase 1; Homo sapiens acyl- Coenzyme A oxidase 1, palmitoyl (ACOX1), transcript variant 1, mRNA.; synonyms: ACOX, PALMCOX, MGC1198; acyl-coenzyme A oxidase 1; Homo sapiens acyl-Coenzyme A oxidase 1, palmitoyl (ACOX1), transcript variant 2, mRNA.
202275_at	G6PD; G6PD; G6PD1	NM_000402	Xq28	Hs.80206	1.327744	Up	0.009288356	1.1621798	Up	0.0824373	synonym: G6PD1; Homo sapiens glucose-6-phosphate dehydrogenase (G6PD), nuclear gene encoding mitochondrial protein, mRNA
208369_s_at	GCDH	NM_013976	19p13.2	Hs.18414 1	1.179371	Up	0.004779557	1.0740528	Up	0.0802765	Homo sapiens glutaryl- Coenzyme A dehydrogenase (GCDH), nuclear gene encoding mitochondrial protein, transcript variant 1, mRNA.; Homo sapiens glutaryl-Coenzyme A dehydrogenase (GCDH), nuclear gene encoding mitochondrial protein, transcript variant 2, mRNA.

219818_x_at	COL5A1	AI082325	11 Hs.38113 4	1.582872 Up	3.02281E-05	1.1263766 Up	0.20423491	ESTs, Moderately similar to RIKEN cDNA 1810059G22 [Mus musculus] [M.musculus] NY-REN-24 antigen
214892_x_at	NY-REN-24	BC004282	Hs.12842 5	1.290886 Up	3.8856E-03	1.0388893 Up	0.49972711	
215558_x_at	HMGCL; HMGCL; HL	AL031285	Hs.931 1p36.1- p35	1.280746 Up	3.92837E-05	1.0334089 Up	0.52753439	synonym: HL; 3-hydroxy-3- methylglutaryl-Coenzyme A lyase; 3-hydroxy-3- methylglutaryl-Coenzyme A lyase (hydroxymethylglutathione); Homo sapiens 3-hydroxymethyl- 3-methylglutaryl-Coenzyme A lyase (hydroxymethylglutathione) (HMGCL), mRNA. synonym: PICOT; PKC- interacting cousin of thiorodoxin; Homo sapiens thiorodoxin-like 2 (TXNL2), mRNA.
207506_at	TXNL2; TXNL2; PICOT	NM_006941	8p25.3 Hs.42644	1.376835 Up	0.005319749	1.0210081 Up	0.88528808	
205236_x_at	SOD3	NM_003102	4p16.3- q21 Hs.2420	1.280517 Up	0.001885857	1.0086441 Up	0.88220478	Homo sapiens superoxide dismutase 3, extracellular (SOD3), mRNA.
203578_at	BCAT2; BCAT2; BCT2	NM_001180	18q13 Hs.10140 6	1.287101 Up	0.000421341	1.0767065 Up	0.19872382	synonym: BCT2; predicted mature protein begins at amino acid 28; Homo sapiens branched chain aminotransferase 2, mitochondrial (BCAT2), mRNA.
208581_x_at	MTIX	NM_005952	16q13 Hs.37495 0	1.547631 Up	0.010241902	1.3216147 Up	0.0043787	synonyms: MT1, MT-1k; Homo sapiens metallothionein 1X (MT1X), mRNA.

patne m et al
(maltrbq)

0.07248872 synonym: P5CD, ALDH4,
P5CDH, P5CDHL, P5CDHS;
aldehyde dehydrogenase 4;
mitochondrial delta-1-pyrroline 5-
carboxylate dehydrogenase;
P5C dehydrogenase; Homo
sapiens aldehyde
dehydrogenase 4 family,
member A1 (ALDH4A1), nuclear
gene encoding mitochondrial
protein, transcript variant
P5CDHL, mRNA; synonyms:
P5CD, ALDH4, P5CDH,
P5CDHL, P5CDHS; aldehyde
dehydrogenase 4; mitochondrial
delta-1-pyrroline 5-carboxylate
dehydrogenase; P5C
dehydrogenase; Homo sapiens
aldehyde dehydrogenase 4
family, member A1 (ALDH4A1),
nuclear gene encoding
mitochondrial protein, transcript
variant P5CDHS, mRNA

0.021809234 1.2649056 Up

H³ 77448 1.432904 Up

NM_003748 1_p36

ALDH4A1;
ALDH4A1;
P5CD; P5CDH;
P5CDH;
P5CDHL;
P5CDHS

200722_at

212185_x_at	MT2A	NM_005953	16q13	Hs.11878 6	1.384172 Up	0.033875359	1.3559748 Up	0.0774698 synonym: MT2; This sequence comes from Fig. 2; Homo sapiens metallothionein 2A (MT2A), mRNA
212859_x_at	MT1E	BF217881	16q13	Hs.43320 5	1.34909 Up	0.012855859	1.2187557 Up	0.023793 metallothionein 1E (functional)
217165_x_at	MT1F; MT1F; MGC32732	M10843	16q13		1.186389 Up	0.225324931	1.2547997 Up	0.0079278 synonyms: MT1, MGC32732; Homo sapiens metallothionein 1F (functional) (MT1F), mRNA
213829_x_at	MT1F	BF248115	15q13	Hs.38189 7	1.120311 Up	0.312657369	1.1895955 Up	0.057089 metallothionein 1F (functional)
201559_at	OAT; OAT; HOGA	NM_008274	10q25	Hs.75485	1.210476 Down	0.003978229	0.8748633 Down	0.1191281 synonym: HOGA; Ornithine aminotransferase; Homo sapiens ornithine aminotransferase (gyrate atrophy) (OAT), nuclear gene encoding mitochondrial protein, mRNA
212481_at	OAZIN	BF783951	8q22.3	Hs.22304 4	1.238532 Down	0.016483367	1.1311716 Down	0.0150402 ornithine decarboxylase antizyme inhibitor
201384_a_at	OAZ2	AF242521	15q22.1	Hs.74553	1.115752 Down	0.079501376	1.1385562 Down	0.0953062 protein translation dependent on +1 ribosomal frameshift; antizyme 2; Homo sapiens ornithine decarboxylase antizyme 2 (OAZ2), mRNA

Ornithine related

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203348_a_at	ARG2	U75997	14q24.3 14q24.3	Hs.17285 1	1.241001 Down	0.006933609	1.1794933 Down	0.0060678 kidney arginase; nonhepatic arginase; L-arginine amidohydrolase; L-arginine ureahydrolase; Arg; Homo sapiens arginase, type II (ARG2), nuclear gene encoding mitochondrial protein, mRNA
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Arginine Related

0.08574831 synonyms: G6a, NG30, DDAHII;
dimethylarginine
dimethylargininohydrolase II;
Homo sapiens dimethylarginine
dimethylaminohydrolase 2
(DDAH2), mRNA.

0.045189089 1.1140322 Up

1.218674 Up

Hs.24738
2

NM_013974 6p21.3

DDAH2;
DDAH2; G6a;
NG30; DDAHII

202282_x_at

0.00155735 synonyms: HO57, VATB, VPP3,
Vma2, ATP8B2, ATP6B1B2;
vacuolar proton pump B isoform
2; endomembrane proton pump
58 kDa subunit; vacuolar ATP
synthase subunit B, brain
isoform; V-ATPase B2 subunit;
H(+)-transporting two-sector
ATPase, 58/58kD subunit,
isoform 2; Homo sapiens
ATPase, H+-transporting,
lysosomal 58/58kDa, V1 subunit
B, isoform 2 (ATP8V1B2),
mRNA.

0.008758781 0.0220404 Down

1.203827 Down

Hs.1697

NM_001693 8p22-p21

ATP8V1B2;
ATP6V1B2;
HO57; VATB;
VPP3; Vma2;
ATP8B2;
ATP6B1B2

201059_at

ATP synthase

201443_g_1	ATP8IP2; ATP8IP2; MB-9; APT6MB-9; ATP6MB-9	AF248988	Xq21	Hs.18343 4	1.138442 Down	0.018987088	0.6876037 Down	0.00772083	synonyms: MB-9, APT6MB-9, ATP8MB-9; ATPase, H ⁺ transporting, lysosomal (vacuolar proton pump) membrane sector associated protein MB-9; vacuolar ATP synthase membrane sector associated protein MB-9; V- ATPase MB.9 subunit; ATPase membrane sector associated protein MB-9; renin receptor; Homo sapiens ATPase, H ⁺ transporting, lysosomal interacting protein 2 (ATP8IP2), mRNA.
201444_g_1	ATP8IP2; ATP8IP2; MB-9; APT6MB-9; ATP6MB-9	NM_005763	Xq21	Hs.18343 4	1.302733 Down	0.012483331	0.7879111 Down	0.01120889	synonyms: MB-9, APT6MB-9, ATP8MB-9; ATPase, H ⁺ transporting, lysosomal (vacuolar proton pump) membrane sector associated protein MB-9; vacuolar ATP synthase membrane sector associated protein MB-9; V- ATPase MB.9 subunit; ATPase membrane sector associated protein MB-9; renin receptor; Homo sapiens ATPase, H ⁺ transporting, lysosomal interacting protein 2 (ATP8IP2), mRNA.

0.01580041 synonyms: VATC, Vma5, ATP8C, ATP8D, FLJ20057; vacuolar proton-ATPase, subunit C, VI domain; H⁺-transporting ATPase chain C, vacuolar, vacuolar proton pump C subunit; H⁺-transporting two-sector ATPase, subunit C; vacuolar ATP synthase subunit C; V-ATPase C subunit; vacuolar proton pump, 42-kD subunit; vat c; H⁺-ATPase C subunit; ATPase, H⁺-transporting, lysosomal, 42kD; ATPase, H⁺-transporting, lysosomal, subunit C; Homo sapiens ATPase, H⁺-transporting, lysosomal 42kDa, V1 subunit C, isoform 1 (ATP6V1C1), mRNA.

0.012519533 0.8194812 Down

1.244045 Down

Hs.86805

NM_001695 8q22.3

ATP6V1C1;

ATP6V1C1;

VATC; Vma5;

ATP8C; ATP8D;

FLJ20057

202874_s_at

0.00501154 synonyms: ATP5, ATPM, ATP5A; ATP synthase, H⁺-transporting (ATPase, mitochondrial); ATP synthase coupling factor 6; Homo sapiens ATP synthase, H⁺-transporting, mitochondrial F0 complex, subunit F6 (ATP5J), nuclear gene encoding mitochondrial protein, mRNA.

0.00088007 0.8948735 Down

1.198518 Down

Hs.73851

NM_001685 21q21.1

ATP5J; ATP5J;

ATPM; ATP5A

207325_s_at

ATP synthase

0.0001404 ATP synthase, mitochondrial, C subunit-3; Homo sapiens ATP synthase, H⁺-transporting, mitochondrial F0 complex, subunit c (subunit 8) isoform 3 (ATP5G3), mRNA.

0.005733489 0.8944746 Down

1.193118 Down

Hs.429

NM_001689 2q31.1

ATP5G3

207507_s_at

(vacuolar)

207508_at	ATP5G3	NM_001689	2q31.1	Hs.429	1.131765 Down	0.034321	0.8651774 Down	0.00239781 ATP synthase, mitochondrial, C subunit-3; Homo sapiens ATP synthase, H+ transporting, mitochondrial F0 complex, subunit c (subunit 3) isoform 3 (ATP5G3), mRNA
208745_at	ATP5L	AA917872	11q23	Hs.10747 8	1.187875 Down	0.011545587	0.8447284 Down	0.00101289 ATP synthase, H+ transporting, mitochondrial F0 complex, subunit g
208870_x_at	ATP5C1; ATP5C1; ATP5CL1	BC000991	10q22-q23	Hs.15543 3	1.124441 Down	0.019343048	0.9124323 Down	0.01392037 synonyms: ATP5C, ATP5CL1; H(heart)-type ATP synthase, gamma-subunit; ATP synthase, H+ transporting, mitochondrial F1 complex, gamma polypeptide like 1; Homo sapiens ATP synthase, H+ transporting, mitochondrial F1 complex, gamma polypeptide 1 (ATP5C1), mRNA
211755_s_at	ATP5F1	BC005980	1p13.1	Hs.81634	1.162553 Down	0.003390778	0.8787885 Down	0.00163431 ATP synthase, H+ transporting, mitochondrial F0 complex, subunit b, isoform 1
213738_s_at	ATP5A1	A1587323	18q12-q21	Hs.40588 5	1.144936 Down	0.009591883	0.8790484 Down	0.00395739 ATP synthase, H+ transporting, mitochondrial F1 complex, alpha subunit, isoform 1, cardiac muscle

Complex 1

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201304_at	NDUFA5; NDUFAB5; B13; NUFM1; UQOR13; FLJ12147; C1- 13KD-B	NM_005000 7q32	Hs.83316	1.251252 Down	0.004319206	0.8538455 Down	0.01854249	synonyms: B13, NUFM, UQOR13, FLJ12147, C1-13KD- B; NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 5 (13kD, B13); Complex I-13KD-B; ubiquinone reductase; type I dehydrogenase; Homo sapiens NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 5, 13kDa (NDUFA5), nuclear gene encoding mitochondrial protein, mRNA.
202001_at	NDUFA6; NDUFAB6; B14	NM_002480 22q13.2- q13.31	Hs.27441 6	1.180897 Down	0.002836277	0.8384038 Down	0.00056884	synonyms: B14; NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 6; NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 6 (14kD, B14); Homo sapiens NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 6, 14kDa (NDUFA6), mRNA.
202077_at	NDUFAB1; NDUFAB1; SDAP	NM_005003	Hs.5553	1.178996 Down	0.001418435	0.8300824 Down	0.000223024	synonyms: SDAP; NDUFAB1 subunit; NADH dehydrogenase (ubiquinone) 1, alpha/beta subcomplex, 1 (8kD, SDAP); Homo sapiens NADH dehydrogenase (ubiquinone) 1, alpha/beta subcomplex, 1, 8kDa (NDUFAB1), mRNA.

203971_s_at	NDUFB3; NDUFB3; B12	NM_002491 2q31.3	Hs.10976 0	1.193323 Down	0.007489942	0.83959 Down	0.00103855 synonym: B12; NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 3 (12kD, B12); Homo sapiens NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 3, 12kDa (NDUFB3), mRNA.
203813_s_at	NDUFB8; NDUFB8; B17	NM_002493	Hs.10964 6	1.138307 Down	0.022389242	0.8259695 Down	0.00038884 synonym: B17; NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 6 (17kD, B17); Homo sapiens NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 6, 17kDa (NDUFB8), mRNA.
203821_at	NDUFB6; NDUFB6; SGDH	NM_002492 3q27.1	Hs.19236	1.151684 Down	0.042430348	0.8851788 Down	0.01813304 synonym: SGDH; NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 5 (16kD, SGDH); Homo sapiens NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 5, 16kDa (NDUFB6), mRNA.
203780_s_at	NDUFB1; NDUFB1; MNLL; CI- SGDH	NM_004545 14q32.12	Hs.18343 5	1.180237 Down	0.004989016	0.8718048 Down	0.00308552 synonym: MNLL, CI-SGDH; NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 1 (7kD, MNLL); Homo sapiens NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 1, 7kDa (NDUFB1), mRNA.

Complex 4	COX7A2	NM_001885	8612	Hs_70312	1.439356	Down	0.007884768	0.665174	Down	1.877E-08	synonyms: COX7AL, COX7AL1, COXVIIa-L, hepatic cytochrome c oxidase chain VIIa; Homo sapiens cytochrome c oxidase subunit VIIa polypeptide 2 (liver)
	COX7A2										[COX7A2], nuclear gene encoding mitochondrial protein, mRNA
	COX7AL										
	COXVIIa-L										
	COX7B	NM_001886	Xq13.2	Hs_43217	1.130844	Down	0.045735159	0.8628608	Down	0.00061257	cytochrome-c oxidase chain VIIb; Homo sapiens cytochrome c oxidase subunit VIIb (COX7B), nuclear gene encoding mitochondrial protein, mRNA
	202110_at										

203663_s_at	COX15A	NM_004255:15q25	Hs.32289	1.197943 Down	0.004378832	0.8135834 Down	7.24025E-04	synonyms: VA, COX, COX-VA; cytochrome c oxidase polypeptide, mitochondrial precursor; Homo sapiens cytochrome c oxidase subunit Va (COX5A), nuclear gene, encoding mitochondrial protein, mRNA
203880_at	COX17	NN_005684	Hs.16287	1.199099 Down	0.014912612	0.8134865 Down	0.000165528	human homolog of yeast mitochondrial copper recruitment gene; COX17 (yeast) homolog, cytochrome c oxidase assembly protein; Homo sapiens COX17 homolog, cytochrome c oxidase assembly protein (yeast) (COX17), nuclear gene encoding mitochondrial protein, mRNA
214277_at	COX11	AI376724	Hs.24151 ₅	1.257888 Down	0.009150553	0.8805178 Down	0.02384433	COX11 homolog, cytochrome c oxidase assembly protein (yeast)
217481_x_at	COX7CP1	AF042165	T3q14-q21	1.448912 Down	0.031232864	0.9438584 Down	0.04448088	cytochrome c oxidase subunit VIIc; E.C. number =1.9.3.1; Homo sapiens cytochrome c oxidase subunit VIIc (COX7CP1) pseudogene, complete sequence
217329_x_at	COX7BP1; bK71497.1	AF042164	22q13	1.228784 Down	0.002837439	1.1251074 Down	0.06248038	cytochrome c oxidase subunit VIIb; E.C. number =1.9.3.1; Homo sapiens cytochrome c oxidase subunit VIIb (COX7BP1) pseudogene, complete sequence

Holocytochrome c Synthetase	HCOB	AI801013	Xq22.3	Hs.21157 ₁	1.168768 Down	0.002771725	0.8395424 Down	0.00635625	holocytochrome c synthase (cytochrome c heme-lyase)
203745_at									

0.01828721 synonym: CCHL; putative;
Homo sapiens holochochrome c
synthase (cytochrome c heme-
lyase) (HCCS), mRNA

0.005742037 1.8000834 Down

1.192373 Down

Hs.21157

NM_005333 Xq22.3

HCCS; HCCS;
CCHL

203748_a_at

0.00413588 synonym: T1-AMT; AMT1;
PEO2; PEO3; adenine
nucleotide translocase 1
(skeletal muscle); Homo sapiens
apoptotic carrier family 25
(mitochondrial carrier; adenine
nucleotide translocator)
member 4 (SLC25A4); nuclear
gene encoding mitochondrial
protein, mRNA

0.003755192 0.3545041 Down

0.242055 Down

Hs.2543

NM_001161 Xq35

SLC25A4;
SLC25A4; T1-
AMT; AMT1;
PEO2; PEO3

202625_at

0.01028424 synonym: GCE, NKH, GCST;
Homo sapiens
aminomethyltransferase (glycine
cleavage system protein T)
(AMT), mRNA

0.003891538 1.4981119 Up

1.28889 Up

Hs.102

NM_000481 3p21.2-
p21.1

AMT; AMT;
GCE; NKH;
GCST

204294_at

Glycine/Serine
Ammonia

0.00348893 Homo sapiens voltage-
dependent anion channel 2
(VDAC2), mRNA
0.0008484 Homo sapiens VDAC1
pseudogene.
0.0287343 synonym: HD-VDAC3; similar to
mouse VDAC 3; Homo sapiens
voltage-dependent anion
channel 3 (VDAC3), mRNA

0.014133989 0.8888017 Down

1.12617 Down

Hs.76802

10p22

VDAC2

211652_at

Voltage dependent
anion channels

0.016102094 0.7707105 Down

1.215466 Down

Hs.7381

AJ002428 Xq21-q22

VDAC1P

217140_s_at

Voltage dependent
anion channels

0.050742358 1.1200838 Down

1.162087 Down

Hs.7381

10p11.2

VDAC3;
VDAC3; HD-
VDAC3

208846_a_at

0.00138614 lactate dehydrogenase B
0.000774 synonym: LDH1; Homo sapiens
lactate dehydrogenase A
(LDHA), mRNA.

0.0010265 Homo sapiens lactate
dehydrogenase B (LDHB),
mRNA.

0.030076971 0.9133205 Down
0.03774559 1.1884595 Down
0.05927145 1.1067107 Down

1.104586 Down
1.134901 Down
1.08357 Down

BE042354	12p12.2- p12.1	Hs.2344B 9
NIM_005566	11p15.4	Hs.2795

LDHB	LDHA; LDHA; LDH1	LDHB
2113584_x_at	200550_a_at	201030_x_at

Lactate metabolism

001918005 9/10/1997 H-1PHB-MG0506
 FLV-HUG3: isoform 1
 hydroxylase, NAD+-specific
 isocitrate dehydrogenase-beta
 precursor, NAD+-specific
 isocitrate dehydrogenase-
 subunit, NAD+-specific (IDB)
 isocitrate dehydrogenase,
 NAD(+)-specific, mitochondrial
 beta subunit, Homo sapiens
 isocitrate dehydrogenase 3
 (NAD+) beta (IDB3B), nuclear
 gene encoding mitochondrial
 protein, transcript variant 1,
 mRNA

610203205 0-051062 10000

He 155-1 - 1,72204 Down

08-148, IDHSB - AF72206 - 2009
 11-DH
 NC200
 ELU1043

biostrate
dehydrogenase

210418_s_at	IDH3B; IDH3B; AF23265	20p13	Hs.15541	1.187509 Down	0.019473713	0.8451559 Down	0.00368348	synonyms: H-IDH3B, MGC9037-FLJ11043; isocitric dehydrogenase; NAD(+)-specific isocitrate dehydrogenase beta precursor; NAD(+)-specific isocitrate dehydrogenase p subunit; NAD(+)-specific (CDH) isocitrate dehydrogenase; isocitrate dehydrogenase (NAD+) specific; mitochondrial beta subunit; Homo sapiens isocitrate dehydrogenase 3 (NAD+) beta (IDH3B)-nuclear gene encoding mitochondrial protein; transcript variant 1; mRNA
202069_s_at	IDH3A	15q25.1-q25.2	Hs.25061	1.42988 Down	0.000595139	0.7382903 Down	0.00167327	isocitrate dehydrogenase 3 (NAD+) alpha
202070_s_at	IDH3A	15q25.1-q25.2	Hs.25061	1.407756 Down	0.0988643023	1.1153047 Down	0.0224165	isocitrate dehydrogenase (NAD) subunit alpha, mitochondrial; NAD(+)-specific (CDH; NAD(+)-specific isocitrate dehydrogenase alpha subunit precursor; isocitrate dehydrogenase (NAD+) alpha chain precursor; H-IDH3A; isocitric dehydrogenase; Homo sapiens isocitrate dehydrogenase 3 (NAD+) alpha (IDH3A); nuclear gene encoding mitochondrial protein; mRNA

HMG related

Accession	Gene	Protein	Length	Score	Expect	Ident	Gap	Frame	Start	Stop	Strand	Feature
21E568_x.at	HMGC1	AL031285	1338	11899	1.237843	Down	0.004508094	0.9568828	Down	0.02046912	Homio sapiens 3-hydroxy-3-methylglutaryl-Coenzyme A reductase (HMGCR), mRNA	synonym: Hs_3-hydroxy-3-methylglutaryl-Coenzyme A lyase; 3-hydroxy-3-methylglutaryl-Coenzyme A lyase (hydroxymethylglutaryl-Coenzyme A lyase)
21E568_x.at	HMGC1	AL031285	1338	11899	1.237843	Down	0.004508094	0.9568828	Down	0.02046912	Homio sapiens 3-hydroxy-3-methylglutaryl-Coenzyme A reductase (HMGCR), mRNA	synonym: Hs_3-hydroxy-3-methylglutaryl-Coenzyme A lyase; 3-hydroxy-3-methylglutaryl-Coenzyme A lyase (hydroxymethylglutaryl-Coenzyme A lyase)

Glutamate metabolism	GLRX2; GLRX2; NM-016986 Ref.12	He 5694	1 214851 Down	0.00065749	0.0182831 Down	U,0001692 synonym: GRX2; thioltransferase; contains nuclear membrane localization GGH-133 protein; Flaming signals plutaredoxin 2 (GLRX2); HBBNA
	219933 pt. GRX2	Ref.12: 9313				

Oxidized	202017_at	EPHX1; EPHX1; NIA_000120 1q42.1	HS.88649	1.406D22 Up	0.66553734 1.4155553 Up	0.622359	synonyms: MEH, EPHX, EPOX; Epoxide hydroxylase 1, microsomal (xenobiotic); Homo sapiens epoxide hydrolase 1, microsomal (xenobiotic) (EPHX1), mRNA
		EPHX1; EPHX1; NIA_000120 1q42.1 MEH; EPOX	HS.88649	1.406D22 Up	0.66553734 1.4155553 Up	0.622359	synonyms: MEH, EPHX, EPOX; Epoxide hydroxylase 1, microsomal (xenobiotic); Homo sapiens epoxide hydrolase 1, microsomal (xenobiotic) (EPHX1), mRNA

Glenn

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Ordering Information

Claims

1. Use of any of the following proteins in a screening assay to identify a potential therapeutic agent for the prevention, treatment, or amelioration of schizophrenia:
(i) proteins encoded by the following genes: PARG; OLR1; ARPC3; ARPC3; DNCL1; PPM1A; ATP1F1; TIMM17A; DNAJA1; SST; NEUROD6; ICAP-1A; FLJ23251; KCNK1; FLJ13611; HIRIP5; TAC1; MAGEH1; C13orf12; EBNA1BP2; DIRAS2; MPPE1; OAT; OAZIN; OAZ2; ARG2; ATP6V1B2; ATP6IP2; ATP6V1C1; ATP5J; ATP5G3; ATP5L; ATP5C1; ATP5F1; ATP5A1; NDUFA5; NDUFA6; NDUFAB1; NDUFB3; NDUFB6; NDUFB5; NDUFB1; NDUFS4; NDUFA4; NDUFC2; NDUFB4; UQCRH; UQCRFS1; UQCRC2; UQCRB; UQCRC2; COX7A2; COX7B; COX5A; COX17; COX11; COX7CP1; COX7BP1; HCCS; SLC25A4; VDAC2; VDAC1P; VDAC3; LDHB; LDHA; IDH3B; IDH3A; HMGCR; GLRX2; FBS1; WFS1; PRODH; AMT; CLN3; ACOX1; G6PD; GCDH; COL5A1; NY-REN-24; TXNL2; SOD3; BCAT2; ALDH4A1; PYCR1; MT1X; MT1L; MT1G; MT1H; MT2A; MT1E; MT1F; DDAH2; AMT; HMGCL; EPHX1; or
ii) nucleic acid encoding any of the proteins of (i) above.
2. Use of a regulator of expression of any of (i) of claim 1, in a screening assay to identify a potential therapeutic agent for the prevention, treatment, or amelioration of schizophrenia.
3. Use of a binding partner of any of (i) of claim 1 in a screening assay to identify a potential therapeutic agent for the prevention, treatment, or amelioration of schizophrenia.
4. Use of an expression vector comprising nucleic acid encoding any of (i) of claim 1 in a screening assay to identify a potential therapeutic agent for the prevention, treatment, or amelioration of schizophrenia.
5. Use of a cell or cell line expressing nucleic acid encoding any of (i) of claim 1 in a screening assay to identify a potential therapeutic agent for the prevention, treatment, or amelioration of schizophrenia.

6. Use according to claim 5, wherein the cell is a neural cell.
7. Use according to claim 5, wherein the cell is an oligodendrocyte.
8. A recombinant mouse in which expression of a gene encoding any of (i) of claim 1 is altered compared with expression of the corresponding gene in normal mice.
9. A recombinant mouse according to claim 8 in which expression of two or more of the genes is altered.
10. A recombinant mouse according to claim 8 or 9 which is a knockout mouse for the gene or genes.
11. Use of a recombinant mouse according to any of claims 8 to 10 as an animal model for schizophrenia.
12. Use of a mouse according to any of claims 8 to 10, or cells obtained or derived from the mouse, in a screening assay to identify a potential therapeutic agent for the prevention, treatment, or amelioration of schizophrenia.
13. A screening assay to identify a potential schizophrenia therapeutic agent for the prevention, treatment, or amelioration of schizophrenia which comprises screening for a modulator of expression of a gene encoding any of the proteins of (i) of claim 1 by: providing a system capable of expressing a gene encoding any of the proteins of (i) of claim 1; maintaining the system under conditions for expression of the gene in the presence and absence of a candidate modulator of expression of the gene; and determining the expression level of the gene in the presence and absence of the candidate modulator.
14. A screening assay according to claim 13, which comprises screening for an upregulator of expression of any of the following:

PARG;OLR1; ARPC3; ARPC3; DNCL1; PPM1A; ATP1F1; TIMM17A; DNAJA1; SST; NEUROD6; ICAP-1A; FLJ23251; KCNK1; FLJ13611; HIRIP5; TAC1; MAGEH1; C13orf12; EBNA1BP2; DIRAS2; MPPE1; OAT; OAZIN; OAZ2; ARG2; ATP6V1B2; ATP6IP2; ATP6V1C1; ATP5J; ATP5G3; ATP5L; ATP5C1; ATP5F1; ATP5A1; NDUFA5; NDUFA6; NDUFAB1; NDUFB3; NDUFB6; NDUFB5; NDUFB1; NDUFS4; NDUFA4; NDUFC2; NDUFB4; UQCRH; UQCRFS1; UQCRC2; UQCRB; UQCRC2; COX7A2; COX7B; COX5A; COX17; COX11; COX7CP1; COX7BP1; HCCS; SLC25A4; VDAC2; VDAC1P; VDAC3; LDHB; LDHA; IDH3B; IDH3A; HMGCR; GLRX2.

15. A screening assay according to claim 13, which comprises screening for a downregulator of expression of any of the following:
FBS1; WFS1; PRODH; AMT; CLN3; ACOX1; G6PD; GCDH; COL5A1; NY-REN-24; TXNL2; SOD3; BCAT2; ALDH4A1; PYCR1; MT1X; MT1L; MT1G; MT1H; MT2A; MT1E; MT1F; DDAH2; AMT; HMGCL; EPHX1.

16. A screening assay to identify a potential schizophrenia therapeutic agent for the prevention, treatment, or amelioration of schizophrenia which comprises screening for a regulator of the activity of any of the proteins of (i) of claim 1 by: contacting the protein with a candidate regulator and determining the activity of the protein in the presence and absence of the candidate regulator.

17. A screening assay according to claim 16, which comprises screening for an enhancer or activator of the activity of any of the following proteins:
PARG;OLR1; ARPC3; ARPC3; DNCL1; PPM1A; ATP1F1; TIMM17A; DNAJA1; SST; NEUROD6; ICAP-1A; FLJ23251; KCNK1; FLJ13611; HIRIP5; TAC1; MAGEH1; C13orf12; EBNA1BP2; DIRAS2; MPPE1; OAT; OAZIN; OAZ2; ARG2; ATP6V1B2; ATP6IP2; ATP6V1C1; ATP5J; ATP5G3; ATP5L; ATP5C1; ATP5F1; ATP5A1; NDUFA5; NDUFA6; NDUFAB1; NDUFB3; NDUFB6; NDUFB5; NDUFB1; NDUFS4; NDUFA4; NDUFC2; NDUFB4; UQCRH; UQCRFS1; UQCRC2; UQCRB; UQCRC2; COX7A2; COX7B; COX5A; COX17; COX11; COX7CP1; COX7BP1; HCCS; SLC25A4; VDAC2; VDAC1P; VDAC3; LDHB; LDHA; IDH3B; IDH3A; HMGCR; GLRX2.

18. A screening assay according to claim 16, which comprises screening for an inhibitor of the activity of any of the following proteins:

FBS1; WFS1; PRODH; AMT; CLN3; ACOX1; G6PD; GCDH; COL5A1; NY-REN-24; TXNL2; SOD3; BCAT2; ALDH4A1; PYCR1; MT1X; MT1L; MT1G; MT1H; MT2A; MT1E; MT1F; DDAH2; AMT; HMGCL; EPHX1.

19. A screening assay to identify a potential schizophrenia therapeutic agent for the prevention, treatment, or amelioration of schizophrenia which comprises screening for a regulator of the interaction of any of the proteins of (i) of claim 1 with a binding partner required for the biological effect of the protein by: contacting the protein with the binding partner in the presence of a candidate regulator, and determining binding of the protein to its binding partner in the presence and absence of the candidate regulator.

20. A screening assay according to claim 19, which comprises screening for an enhancer of the interaction of any of the following proteins with a binding partner required for the biological effect of the protein:

PARG; OLR1; ARPC3; ARPC3; DNCL1; PPM1A; ATP1F1; TIMM17A; DNAJA1; SST; NEUROD6; ICAP-1A; FLJ23251; KCNK1; FLJ13611; HIRIP5; TAC1; MAGEH1; C13orf12; EBNA1BP2; DIRAS2; MPPE1; OAT; OAZIN; OAZ2; ARG2; ATP6V1B2; ATP6IP2; ATP6V1C1; ATP5J; ATP5G3; ATP5L; ATP5C1; ATP5F1; ATP5A1; NDUFA5; NDUFA6; NDUFAB1; NDUFB3; NDUFB6; NDUFB5; NDUFB1; NDUFS4; NDUFA4; NDUFC2; NDUFB4; UQCRH; UQCRFS1; UQCRC2; UQCRB; UQCRC2; COX7A2; COX7B; COX5A; COX17; COX11; COX7CP1; COX7BP1; HCCS; SLC25A4; VDAC2; VDAC1P; VDAC3; LDHB; LDHA; IDH3B; IDH3A; HMGCR; GLRX2.

21. A screening assay according to claim 19, which comprises screening for an inhibitor of the interaction of any of the following proteins with a binding partner required for the biological effect of the protein:

FBS1; WFS1; PRODH; AMT; CLN3; ACOX1; G6PD; GCDH; COL5A1; NY-REN-24; TXNL2; SOD3; BCAT2; ALDH4A1; PYCR1; MT1X; MT1L; MT1G; MT1H; MT2A; MT1B; MT1F; DDAH2; AMT; HMGCL; EPHX1.

22. A screening assay to identify a potential schizophrenia therapeutic agent for the prevention, treatment, or amelioration of schizophrenia which comprises screening for a binding partner of any of the proteins of (i) of claim 1 by: contacting the protein with a sample comprising a candidate binding partner, and determining whether the candidate binding partner binds to the protein.

23. A method of diagnosing whether a subject has, or is at risk of developing schizophrenia, which comprises determining the level of any of the proteins of (i) of claim 1, or the expression level of a gene encoding any of the proteins of (i) of claim 1, in a biological sample obtained from the subject, or in a sample derived from a biological sample obtained from the subject.

24. A method according to claim 23, wherein the biological sample comprises a peripheral tissue or cell type in which the level of the protein, or the expression level of the gene, correlates with the level of the corresponding protein, or the expression level of the corresponding protein, in the prefrontal cortex.

25. A method according to claim 24, wherein the peripheral tissue or cell type comprises a blood cell.

26. A method according to claim 25, wherein the blood cell is a macrophage, a monocyte, a lymphocyte, an erythrocyte, a platelet, a leukocyte (either a neutrophil, an eosinophil, or a basophil; a lymphocyte, or a monocyte).

27. A method of prevention, treatment, or amelioration of schizophrenia which comprises increasing the level or activity of any of the following proteins in the brain (in particular the prefrontal cortex) of a subject in need of such prevention, treatment, or amelioration:

PARG; OLR1; ARPC3; ARPC3; DNCL11; PPM1A; ATP1F1; TMM17A; DNAJA1;
SST; NEUROD6; ICAP-1A; FLJ23251; KCNK1; FLJ13611; HIRIP5; TAC1;
MAGEH1; C13orf12; EBNA1BP2; DIRAS2; MPPE1; OAT; OAZIN; OAZ2; ARG2;
ATP6V1B2; ATP6IP2; ATP6V1C1; ATP5J; ATP5G3; ATP5L; ATP5C1; ATP5F1;
ATP5A1; NDUFA5; NDUFA6; NDUFAB1; NDUFB3; NDUFB6; NDUFB5;
NDUFB1; NDUFS4; NDUFA4; NDUFC2; NDUFB4; UQCRC; UQCRCF1;
UQCRC2; UQCRB; UQCRC2; COX7A2; COX7B; COX5A; COX17; COX11;
COX7CP1; COX7BP1; HCCS; SLC25A4; VDAC2; VDAC1P; VDAC3; LDHB;
LDHA; IDH3B; IDH3A; HMGCR; GLRX2.

28. A method of prevention, treatment, or amelioration of schizophrenia which comprises reducing the level or activity of any of the following proteins in the brain (in particular the prefrontal cortex) of a subject in need of such prevention, treatment, or amelioration:

or amelioration:
FBS1; WFS1; PRODH; AMT; CLN3; ACOX1; G6PD; GCDH; COL5A1; NY-REN-
24; TXNL2; SOD3; BCAT2; ALDH4A1; PYCR1; MT1X; MT1L; MT1G; MT1H;
MT2A; MT1E; MT1F; DDAH2; AMT; HMGCL; EPHX1.

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Figure 2

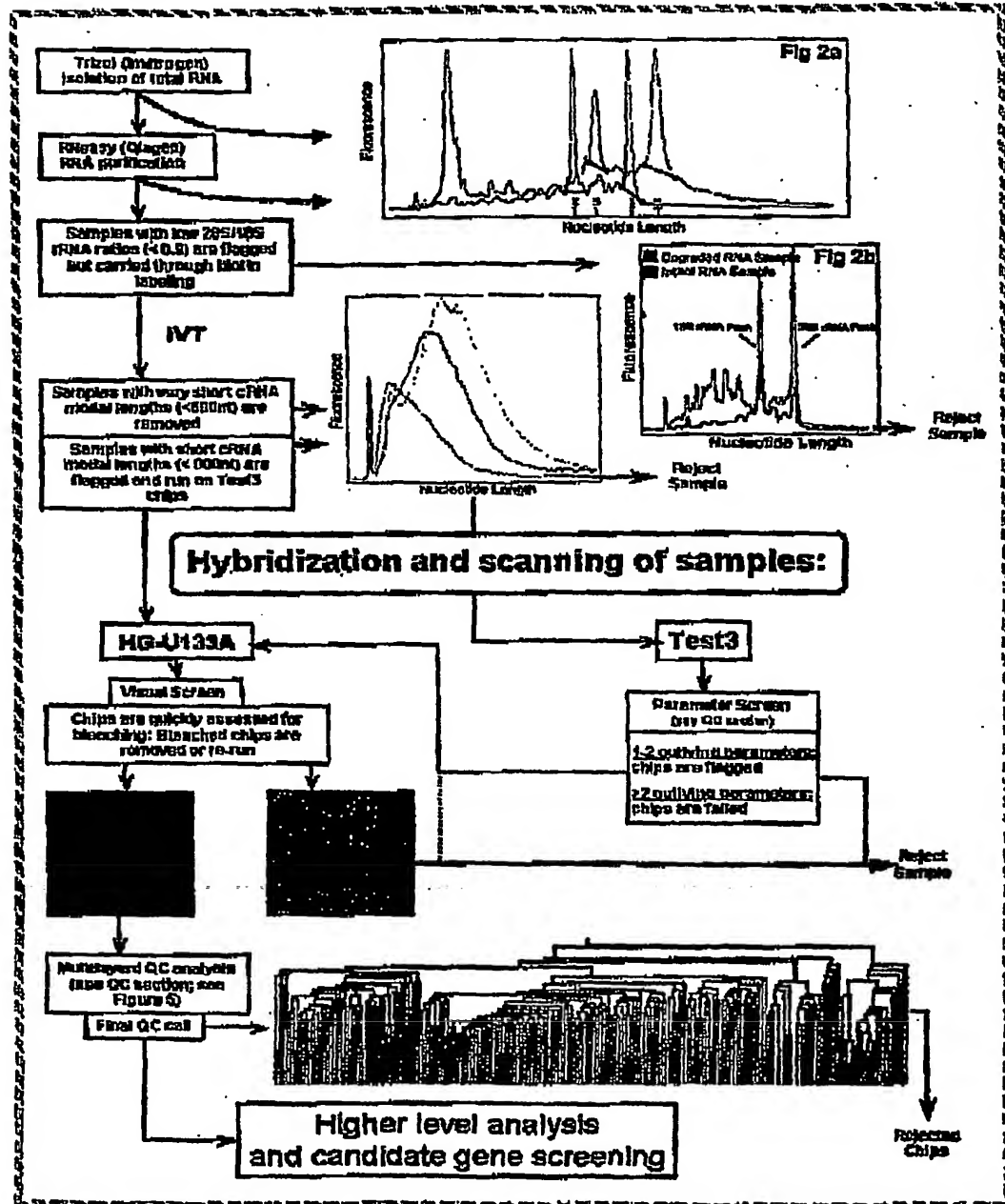
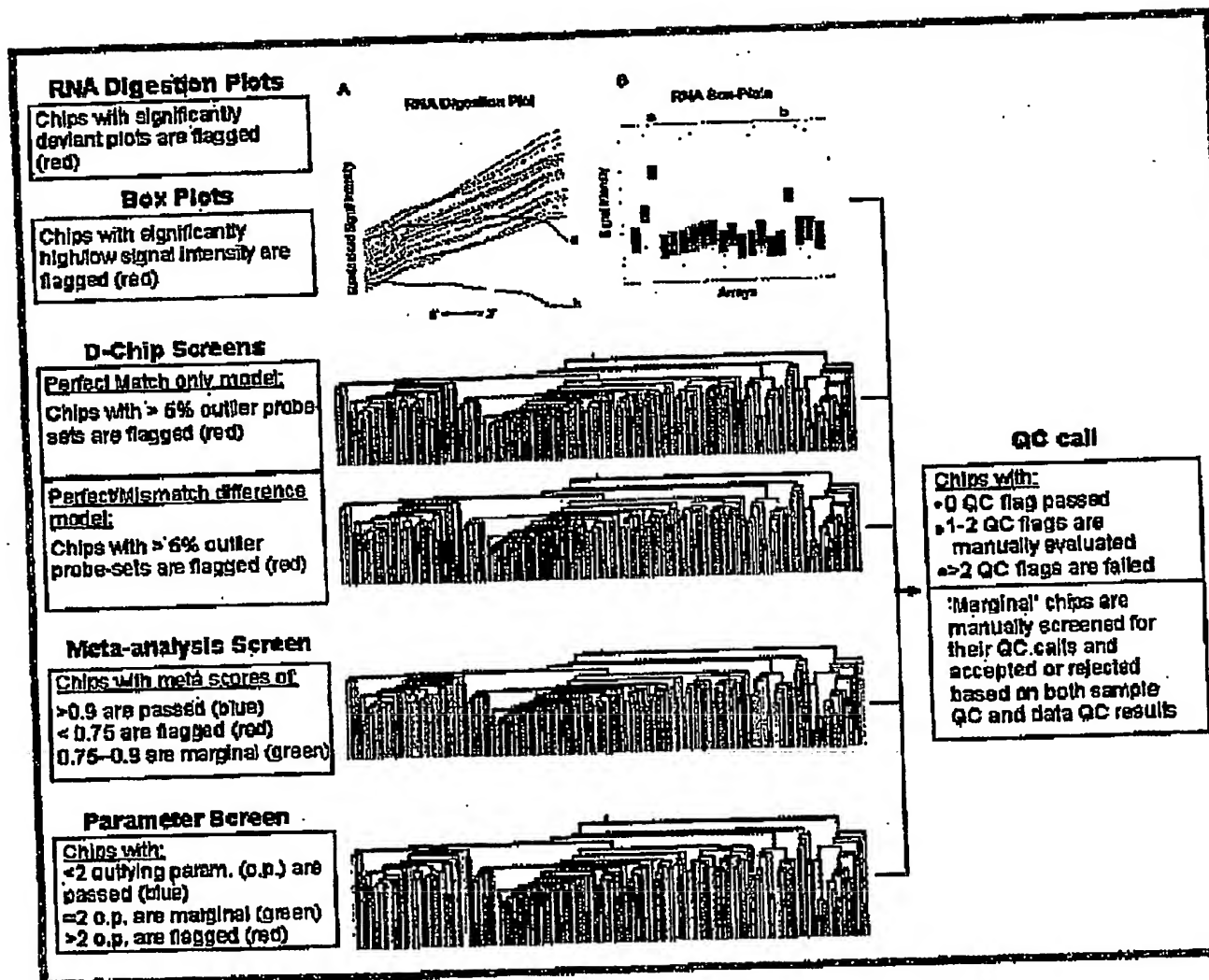


Figure 3



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Figure 4



Schizophrenia **Control**

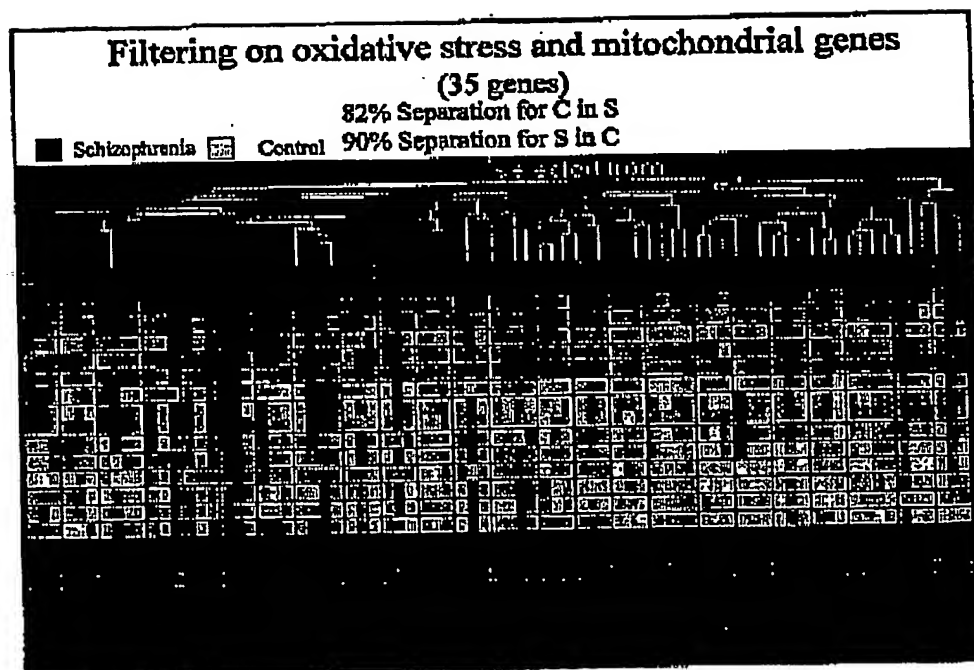
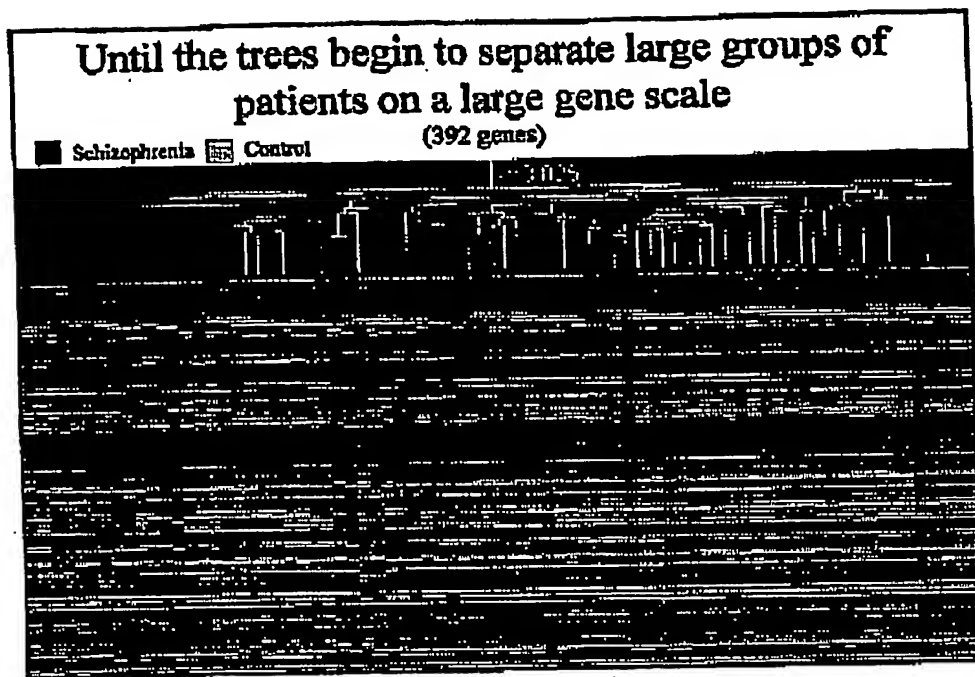
Sign up in



Schizophrenia Control

sig change.

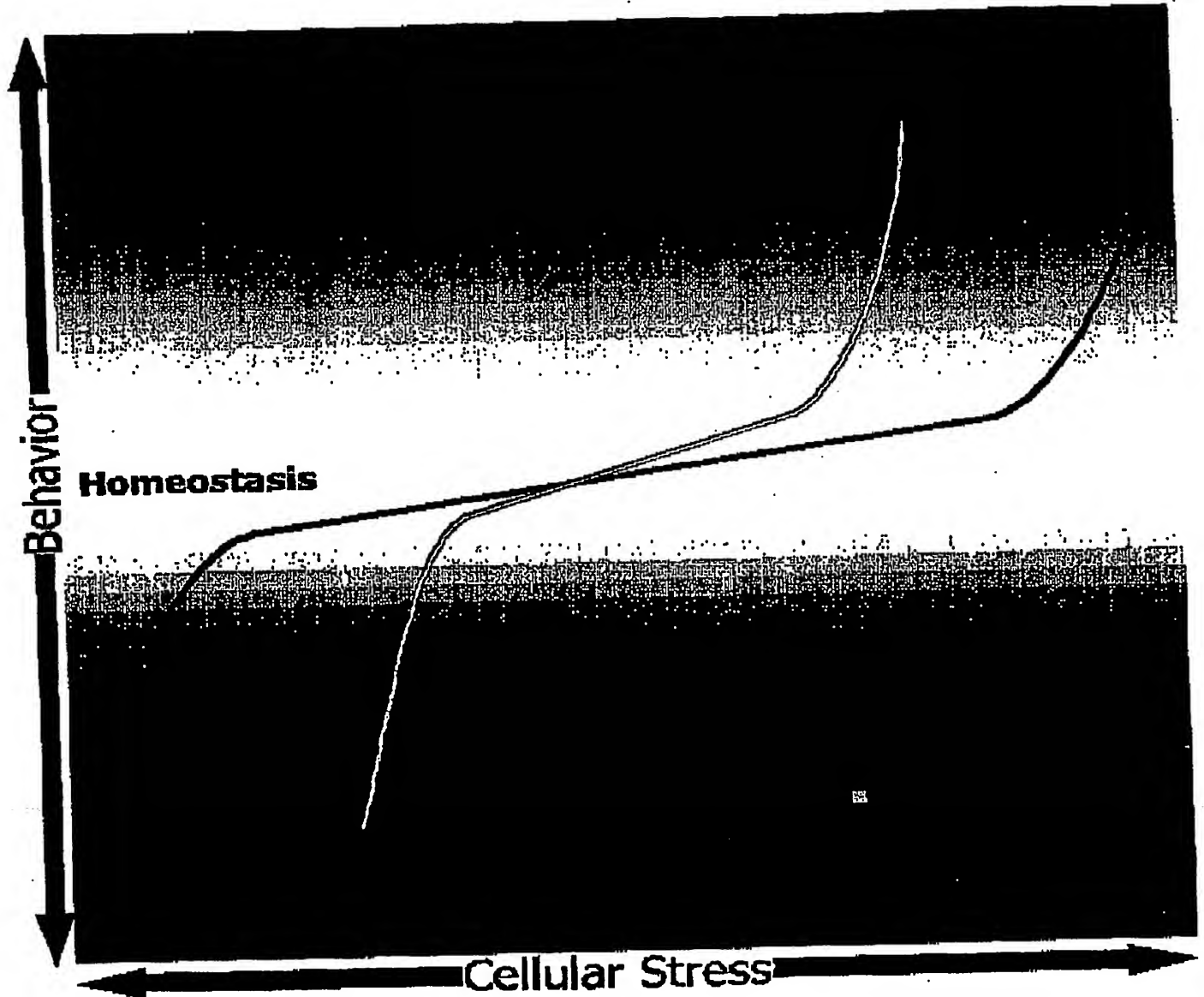
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Figure 5



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Figure 6

Oxidative Buffering



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